

NIOSH

Current Intelligence Bulletin 19

January 13, 1978

2,4 - DIAMINOANISOLE

(4-METHOXY-m-PHENYLENEDIAMINE)

IN HAIR AND FUR DYES



U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

The Current Intelligence Bulletin is the primary product of the Current Intelligence System. The purpose of the Current Intelligence System is to promptly review, evaluate, and supplement new information received by NIOSH on occupational hazards that are either unrecognized or are greater than generally known.

As warranted by this evaluation, the information is capsulized and disseminated to NIOSH staff, other government agencies, and the occupational health community, including labor, industry, academia, and public interest groups. With respect to currently known hazard information this system also serves to advise appropriate members of the above groups of recently acquired specific knowledge which may have an impact on their programs or perception of the hazard. Above all, the Current Intelligence System is designed to protect the health of American workers and to allow them to work in the safest possible environment.

SYNONYMS

2,4-Diaminoanisole

Chemical Abstract Service Number 615-05-4
CI. 76050
CI. Oxidation Base 12
1,3-Diamino-4-methoxybenzene
Furro L
4-Methoxy-1,3-benzenediamine
4-Methoxy-*m*-phenylenediamine
Pelagol DA
Pelagol Grey L
Pelagol L

2,4-Diaminoanisole Sulfate

Chemical Abstract Service Number 39156-41-7
CI. 76051
1,3-Diamino-4-methoxybenzene Sulfate
4-Methoxy-1,3-benzenediamine Sulfate
4-Methoxy-*m*-phenylenediamine Sulfate

DHEW (NIOSH) Publication No. 78-111

CURRENT INTELLIGENCE BULLETIN:

2,4-Diaminoanisole in Hair and Fur Dyes

January 13, 1978

The National Institute for Occupational Safety and Health (NIOSH) recommends that 2,4-diaminoanisole (4-methoxy-m-phenylenediamine) and its salts* be handled in the workplace as if they were human carcinogens. This recommendation is based primarily upon a preliminary analysis of National Cancer Institute data indicating laboratory rats and mice fed 2,4-diaminoanisole sulfate experienced a statistically significant excess of site-specific malignant tumors as compared to controls. Caution is also indicated by NIOSH epidemiologic studies which suggest an elevated incidence of cancer among cosmetologists. As an interim measure, pending further evaluation of the carcinogenic potential of 2,4-diaminoanisole in the workplace, NIOSH believes it would be prudent to minimize occupational exposure to 2,4-diaminoanisole.

This Bulletin summarizes the results of the National Cancer Institute animal study, the NIOSH epidemiologic studies, other pertinent data, their implications for occupational health, and precautions for handling products containing 2,4-diaminoanisole in the workplace.

Background

The principal use of 2,4-diaminoanisole is as a component of oxidation ("permanent") hair and fur dye formulations. Approximately three-quarters of the current oxidation hair dye formulations contain 2,4-diaminoanisole in concentrations ranging from approximately 0.05% to approximately 2%. The concentration is determined by the shade of the dye. Oxidation hair dyes are very common among professional as well as over-the-counter products and account for approximately \$200 million of the \$280 million annual retail expenditure for hair dyes. NIOSH is unaware of any current domestic production of 2,4-diaminoanisole. Imports of 2,4-diaminoanisole are on the order of 25,000 pounds per year.

* In this Bulletin, the phrase, "2,4-diaminoanisole," will be used to signify 2,4-diaminoanisole as well as its salts, such as 2,4-diaminoanisole sulfate (4-methoxy-m-phenylenediamine sulfate).

Potential Occupational Exposures

NIOSH estimates that approximately 400,000 workers have potential occupational exposure to 2,4-diaminoanisole. Hairdressers and cosmetologists comprise the largest portion of workers with potential exposure. (Gloves are usually worn by hairdressers when applying hair dyes). A relatively small number of fur dyers are probably exposed to higher levels of 2,4-diaminoanisole.

Epidemiologic Studies

NIOSH has conducted two epidemiologic studies which suggest excess cancer among cosmetologists.

A report¹ based on data from a case-control study of 25,416 hospital admissions between 1956 and 1965 at Roswell Park Memorial Institute suggests an excess of cancer of specific genital sites (corpus uteri, ovaries) among hairdressers and cosmetologists.

Another study currently being conducted by NIOSH is also suggestive of excess cancer among cosmetologists. This study involves a sample of 53,183 records which are representative of the 417,795 Social Security disability awards made to female workers between 1969 and 1972. Age and race adjusted proportional morbidity ratios* (PMbR's) have been constructed for 24 selected occupational groups. Among cosmetologists, elevated PMbR's were observed for cancer of the digestive organs, respiratory system, trachea, bronchus and lung, breast, and genital organs. Cosmetologists had a greater number of elevated PMbR's for specific primary malignant neoplasms than any other tabulated occupational group. Thus, the preliminary analysis of the Social Security Administration disability data is consistent with the hypothesis that persons employed in occupations classified within the broad category of cosmetology may be at elevated risks of developing a neoplasm due to exposures of occupational origin.

Other relevant epidemiologic studies with conflicting results have been reported.²⁻⁶ These studies do not clearly demonstrate an association between hair dyes and cancer. NIOSH believes that its studies do suggest an association between cancer and employment as cosmetologists and hairdressers. However, it is recognized that cosmetologists and hairdressers are exposed to a large variety of substances, and it is difficult at this time to attribute any excess incidence of cancer to either hair dyes in general or 2,4-diaminoanisole in particular.

* Each proportional morbidity ratio compares the observed number of women within an occupational category granted an award for a particular disability with the expected number of women (derived from all occupations in the entire sample) granted an award for the same disability.

Laboratory Studies

Preliminary analyses of National Cancer Institute data indicate that male and female laboratory rats and mice fed 2,4-diaminoaniline sulfate in their diets for seventy-eight weeks experienced a statistically significant excess of site-specific malignant tumors as compared to controls.

Groups of fifty male and fifty female Fisher 344 rats and B6C3F1 mice were used in the test. Feed containing 0.05% or 0.12% technical grade 2,4-diaminoaniline sulfate was administered to each group of treated rats; each group of treated mice received feed containing 0.12% or 0.24% technical grade 2,4-diaminoaniline sulfate. Fifty animals of each sex of each species served as controls. After the seventy-eight week treatment period, observation of the mice continued for an additional thirteen weeks and observation of the rats continued for an additional twenty-six weeks.

Significant excess cancer was observed in the thyroid gland and integumentary system (skin) of high dose exposed rats of both sexes, as well as in the thyroid gland of high dose exposed mice, and in the lymphatic system of low dose exposed mice.

In other studies, 2,4-diaminoaniline was tested by skin application to laboratory rodents. Testing by skin application has considerable merit since this route of administration approximates that resulting from the use of hair dyes. Laboratory mice and rats painted with 2,4-diaminoaniline have been reported to experience no statistically significant excess of cancer.^{7,8} Kinkle and Holzman, for example, reported applying a mixture containing 0.4% 2,4-diaminoaniline to the shaved backs of Sprague-Dawley rats twice weekly for two years, and then continuing to observe the surviving animals for an additional six months.⁸ However, the interpretation of the reported data is complicated by experimental design⁹ and these experiments do not convincingly establish the safety of 2,4-diaminoaniline applied to skin.

NIOSH understands that recent and still unpublished data acquired by the Food and Drug Administration indicate that 2,4-diaminoaniline penetrates the skin and thereby enters the system of both man and rhesus monkey. This indicates that skin contact with 2,4-diaminoaniline must be avoided in the workplace.

There are reports indicating that 2,4-diaminoaniline is mutagenic in bacterial systems⁹ and in drosophila.¹⁰ Mutagenic activity *per se* should be considered an important liability. In addition, empirical correlations have suggested a relationship between mutagenicity, especially in bacterial strains, and carcinogenicity in higher animals.

NIOSH Recommendation

Animal studies are valuable in helping identify human carcinogens. Substances that cause cancer in experimental animals must be considered to pose a potential cancer risk in man. Although safe levels of exposure to carcinogens have not yet been demonstrated, decreasing exposure to carcinogens does reduce their probability of initiating cancer development.

While the carcinogenicity of 2,4-diaminoaniline is being further evaluated, the National Institute for Occupational Safety and Health recommends, as an interim and prudent measure, that occupational exposure to 2,4-diaminoaniline and its salts be minimized. Exposures should be limited to as few employees as possible, while minimizing workplace exposure levels with engineering and work practice controls. In particular, skin exposures should be avoided. Although substitution is a possible control measure, NIOSH recommends that caution be exercised in selecting a substitute for hair and fur dye formulations containing 2,4-diaminoaniline. Alternatives should be fully evaluated with regard to possible human health effects. This is particularly important in view of the many questions which have been raised recently regarding the safety of numerous components of hair dye formulations.



Edward J. Baier
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References

1. A Retrospective Survey of Cancer in Relation to Occupation, DHEW (NIOSH) Publication No. 77-178, U.S. Department of Health, Education, and Welfare, Public Health Service, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio, 1977.
2. Garfinkel J., Selvin, S. and Brown, S. M., "Possible Increased Risk of Lung Cancer Among Beauticians," J. National Cancer Institute, 58, 141, 1977.
3. Hammond, E. C., "Some Negative Findings (Polio, Small Pox, Tetanus and Diphtheria-Vaccines; Beauticians) and Evaluation of Risks," Presented at the American Cancer Society's Nineteenth Science Writers' Seminar, Sarasota, Florida, April 1977.
4. Kinlen, L. J. et al., "Use of Hair Dyes by Patients with Breast Cancer: A Case-Control Study," British Medical Journal, 2, 366, 1977.
5. Menck, H. R. et al., "Lung Cancer Risk Among Beauticians and Other Female Workers," J. National Cancer Institute, 59, 1423, 1977.
6. Shafer, N., and Shafer, R. W., "Potential of Carcinogenic Effects of Hair Dyes," New York State Journal of Medicine, 76, 394, 1976.
7. Burnett, C. et al., "Long-Term Toxicity Studies on Oxidation Hair Dyes," Food and Cosmetics Toxicology, 13, 353, 1975.
8. Kinkel, H. J., and Holzmann, S., "Study of Long-Term Percutaneous Toxicity and Carcinogenicity of Hair Dyes (Oxidizing Dyes) in Rats," Food and Cosmetics Toxicology, 11, 641, 1973.
9. Ames, B.N. et al., "Hair Dyes Are Mutagenic: Identification of a Variety of Mutagenic Ingredients," Proceedings National Academy of Sciences USA, 72, 2423, 1975.
10. Blijleven, W. G. .H, "Mutagenicity of Four Hair Dyes in Drosophila Melanogaster," Mutation Research, 48, 181, 1977.

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